General

Guideline Title

HER2 testing and clinical decision making in gastroesophageal adenocarcinoma: guideline from the College of American Pathologists, American Society for Clinical Pathology, and American Society of Clinical Oncology.

Bibliographic Source(s)

Bartley AN, Washington MK, Colasacco C, Ventura CB, Ismaila N, Benson AB III, Carrato A, Gulley ML, Jain D, Kakar S, Mackay HJ, Streutker C, Tang L, Troxell M, Ajani JA. HER2 testing and clinical decision making in gastroesophageal adenocarcinoma: guideline from the College of American Pathologists, American Society for Clinical Pathology, and the American Society of Clinical Oncology. J Clin Oncol. 2017 Feb 1;35(4):446-64. [131 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Definitions for the rating of the quality of evidence (High, Moderate, Low, Very low) and the strength of recommendations (Strong recommendation, Recommendation, Expert consensus opinion, No recommendation) are provided at the end of the "Major Recommendations" field.

Clinical Question 1

What is the optimal testing algorithm for the assessment of *human epidermal growth factor receptor 2* (*HER2*) status in patients with gastroesophageal adenocarcinoma (GEA)?

Recommendation 1.1

In patients with advanced GEA who are potential candidates for *HER2*-targeted therapy, the treating clinician should request *HER2* testing on tumor tissue (Type: evidence based; Quality of evidence: high; Strength of recommendation: strong).

Recommendation 1.2

Treating clinicians or pathologists should request *HER2* testing on tumor tissue in the biopsy or resection specimens (primary or metastasis), preferably before the initiation of trastuzumab therapy if such specimens are available and adequate. *HER2* testing on fine needle aspiration (FNA) specimens (cell blocks) is an acceptable alternative (Type: evidence based; Quality of evidence: moderate/intermediate; Strength of

recommendation: recommendation/moderate).

Recommendation 1.3

Treating clinicians should offer combination chemotherapy and *HER2*-targeted therapy as the initial treatment for appropriate patients with *HER2*-positive tumors who have advanced GEA (Type: evidence based; Quality of evidence: moderate/intermediate; Strength of recommendation: strong).

Clinical Question 2

What strategies can help ensure optimal performance, interpretation, and reporting of established assays in patients with GEA?

Recommendation 2.1

Laboratories and pathologists must specify the antibodies and probes used for the test and ensure that assays are appropriately validated for *HER2* immunohistochemistry (IHC) testing and in situ hybridization (ISH) testing on GEA specimens (Type: evidence based; Quality of evidence: moderate/intermediate; Strength of recommendation: strong).

Recommendation 2.2

When GEA *HER2* status is being evaluated, laboratories and/or pathologists should order IHC testing first followed by ISH when IHC result is 2+ (equivocal). Positive (3+) or negative (0 or 1+) *HER2* IHC results do not require further ISH testing (Type: evidence based; Quality of evidence: high; Strength of recommendation: strong).

Recommendation 2.3

Pathologists should use the Ruschoff/Hofmann method in scoring *HER2* IHC and ISH results for GEA (Type: evidence based; Quality of evidence: moderate/intermediate; Strength of recommendation: strong).

Recommendation 2.4

Pathologists should select the tissue block with the areas of lowest grade tumor morphology in biopsy and resection specimens. More than one tissue block may be selected if different morphologic patterns are present (Type: evidence based; Quality of evidence: moderate/intermediate; Strength of recommendation: recommendation/moderate).

Recommendation 2.5

Laboratories should report *HER2* test results in GEA specimens in accordance with the College of American Pathologists (CAP) Template for Reporting Results of *HER2 (ERBB2)* Biomarker Testing of Specimens From Patients With Adenocarcinoma of the Stomach or Esophagogastric Junction (Type: evidence based; Quality of evidence: moderate/intermediate; Strength of recommendation: strong).

Recommendation 2.6

Pathologists should identify areas of invasive adenocarcinoma and also mark areas with strongest intensity of *HER2* expression by IHC in GEA specimens for subsequent ISH scoring when required (Type: evidence based; Quality of evidence: moderate/intermediate; Strength of recommendation: strong).

Recommendation 2.7

Laboratories must incorporate GEA *HER2* testing methods into their overall laboratory quality improvement program, establishing appropriate quality improvement monitors as needed to ensure consistent performance in all steps of the testing and reporting process. In particular, laboratories performing GEA *HER2* testing should participate in a formal proficiency testing program, if available, or an alternative proficiency assurance activity (Type: evidence based; Quality of evidence: moderate/intermediate; Strength of recommendation: strong).

Recommendation 2.8

There is insufficient evidence to recommend for or against genomic testing in GEA patients at this time.

Definitions

Quality of Evidence Ratings in the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Framework

GRADE	Definition
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very low	Any estimate of effect is very uncertain.

Note: Adapted by permission from BMJ Publishing Group Limited. Guyatt GH, Oxman AD, Vist GE, et al: GRADE Working Group: GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. BMJ 336:924-6, 2008. ©2008

Strength of Recommendations

CAP Designation	GLIDES Designation	Recommendation	Rationale
Strong recommendation	Strong	Recommend for or against a particular practice (can include must or should)	Supported by high (convincing) or intermediate (adequate) quality of evidence and clear benefit that outweighs any harms.
Recommendation	Moderate	Recommend for or against a particular practice (can include should or may)	Some limitations in quality of evidence (intermediate [adequate] or low [inadequate]), balance of benefits and harms, values, or costs, but panel concludes that there is sufficient evidence and/or benefit to inform a recommendation.
Expert consensus opinion	Weak	Recommend for or against a particular practice (can include should or may)	Serious limitations in quality of evidence (low [inadequate] or insufficient), balance of benefits and harms, values or costs, but panel consensus is that a statement is necessary.
No recommendation	N/A	No recommendation for or against a particular practice	Insufficient evidence or agreement of the balance of benefits and harms, values, or costs to provide a recommendation.

Note: Data derived from Guyatt GH, Oxman AD, Vist GE, et al: GRADE Working Group: GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. BMJ 336:924-6, 2008.

Abbreviations: CAP, College of American Pathologists; GLIDES, Guidelines Into Decision Support; N/A, not applicable.

Clinical Algorithm(s)

The following algorithms are provided in the original guideline document:

- Algorithm for clinicians
- Algorithm for pathologists

Scope

Disease/Condition(s)

Gastroesophageal adenocarcinoma (GEA)

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Gastroenterology

Oncology

Pathology

Intended Users

Advanced Practice Nurses

Clinical Laboratory Personnel

Patients

Physician Assistants

Physicians

Guideline Objective(s)

- To establish an evidence-based guideline for *human epidermal growth factor receptor 2* (*HER2*) testing in patients with gastroesophageal adenocarcinoma (GEA)
- To formalize the algorithms for methods to improve the accuracy of *HER2* testing while addressing which patients and tumor specimens are appropriate
- To provide guidance on clinical decision making

Target Population

Patients with advanced gastroesophageal adenocarcinoma (GEA)

Interventions and Practices Considered

1. *Human epidermal growth factor receptor 2* (*HER2*) testing on tumor tissues before initiation of *HER2*-targeted therapy
2. *HER2*-targeted therapy (trastuzumab) in combination with chemotherapy
3. Technical issues for pathology laboratories
    - Specification of antibodies and probes used for testing
    - Ensuring that tests are validated for *HER2* immunohistochemistry (IHC) and in situ hybridization (ISH)
    - Order of testing
    - Scoring methods
    - Selection of neoplastic tissue for testing based on morphology
    - Interpretation and reporting of results
    - Laboratory quality assurance

Major Outcomes Considered

- Survival outcomes, including:

- Overall survival (OS)
- Disease-free survival (DFS)
- Progression free survival (PFS)
- Response rate
- Recurrence-free survival
- Time to recurrence
- Response to therapy (e.g., complete and partial response)

- Performance characteristics of laboratory testing assays, including:
  - Sensitivity and specificity of testing methods
  - Concordance

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Systematic Literature Review and Analysis

A systematic literature search was completed for relevant evidence by using OvidSP, PubMed, and Scopus (January 1, 2008, to June 1, 2015). The search strategy included medical subject headings (MeSH) and text words to capture the general concepts of gastroesophageal neoplasms, human epidermal growth factor receptor 2 (*ERBB2/HER2*), targeted therapy, and laboratory testing methods. Database searches were supplemented with a search for unindexed literature, including a review of clinical trials and pertinent organizations' Web sites. All searches were limited to human studies. Expert Panel recommendations and a review of reference lists of included articles for relevant reports completed the systematic literature review. Detailed information regarding the literature search strategy can be found in the Data Supplement (see the "Availability of Companion Documents" field).

Eligible Study Designs

Eligible study designs were determined a priori on the basis of whether they were clinical or laboratory-based studies. Clinical studies were included if they were systematic reviews with or without meta-analyses, guidelines, consensus statements, or randomized controlled trials (except for phase I trials). Additional study types were included for laboratory-based studies due to concern that relevant data would not otherwise be captured. Detailed information about included study designs is available in the Data Supplement.

Inclusion Criteria

Published studies were selected for inclusion in the systematic review of evidence if they met the following criteria: (1) the study included human subjects; (2) the study population consisted of patients with invasive gastroesophageal adenocarcinoma (GEA); (3) the study was published in English; (4) the study compared, prospectively or retrospectively, laboratory testing methodologies or potential testing algorithms for *HER2* testing; (5) the study addressed one of the key questions; and (6) the study included measurable data such as the negative predictive value or positive predictive value of in situ hybridization (ISH) and immunohistochemistry (IHC) assays used to determine *HER2* status, alone and in combination; negative and positive concordance across the platforms; and sensitivity and specificity of individual tests and accuracy in determining *HER2* status. Detailed information about the inclusion criteria is available in the Data Supplement.

Exclusion Criteria

Articles were excluded from the systematic review if they were meeting abstracts that were not published in peer-reviewed journals;

noncomparative or qualitative studies, including editorials, commentaries, and letters; animal studies; full-text articles not available in English; studies that included patients with other tumor types, including esophageal squamous cell carcinoma, or patients with noninvasive tumors; studies that did not include relevant measurable data; and studies that did not address at least one of the key questions. Detailed information about the exclusion criteria is available in the Data Supplement.

Number of Source Documents

A total of 969 studies met the search term requirements. A total of 116 articles were included for data extraction. This consisted of one systematic review, two meta-analyses, two randomized controlled trials, 27 prospective studies, 69 prospective-retrospective studies, and 15 retrospective studies. Excluded articles were available as discussion or background references.

See the Literature Review Flow Diagram (Supplemental Figure 3) in the Data Supplement (see the "Availability of Companion Documents" field) for an outline of the study selection process.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence Ratings in the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Framework

GRADE	Definition
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very low	Any estimate of effect is very uncertain.

Note: Adapted by permission from BMJ Publishing Group Limited. Guyatt GH, Oxman AD, Vist GE, et al: GRADE Working Group: GRADE: An emerging consensus on rating quality of evidence and strength of recommendations. BMJ 336:924-6, 2008. ©2008

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Extraction and Management

Full text articles were reviewed for relevancy by two expert panel members to determine eligibility, and conflicts were resolved by the initial reviewers and further adjudicated by a project co-chair, if necessary. In cases of duplication of reporting study results, the most inclusive were retained. Articles advanced to data extraction if they addressed at least one of the key questions, contained measurable data, and were within the project's scope and met the previously described inclusion/exclusion criteria. Data extraction was performed by a methodologist and audited by one expert panel member. Any discrepancies in data extraction were resolved by discussion. A bibliographic database was established in DistillerSR and EndNote (Thomson Reuters, Carlsbad, CA) to track all literature identified and reviewed during the study.

Quality Assessment Methods

An assessment of the quality of the evidence was performed for all retained studies following application of the inclusion and exclusion criteria.

Using this method, studies deemed to be of low quality would not be excluded from the systematic review, but would be retained and their methodological strengths and weaknesses discussed where relevant. Studies would be assessed by confirming the presence of items related to both internal and external validity, and which are all associated with methodological rigor and a decrease in the risk of bias. These items were assessed as being either yes, no, partial, not reported (NR), or not applicable (N/A) using the methodology detailed in the Data Supplement (see the "Availability of Companion Documents" field).

The Expert Panel rated the quality of evidence for the recommendations as high, moderate/intermediate, low, or insufficient. The Grading of Recommendations Assessment, Development and Evaluation or (GRADE) method was used to rate the quality of the evidence (see the "Rating Scheme for the Strength of the Evidence" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Nominal Group Technique)

Description of Methods Used to Formulate the Recommendations

In 2007, a joint Expert Panel convened by the American Society of Clinical Oncology (ASCO) and the College of American Pathologists (CAP) met to develop guidelines for when and how to test for *human epidermal growth factor receptor 2* (*HER2*) in patients with breast cancer, which is amplified and/or overexpressed in up to 30% of cases. In 2012, ASCO and CAP convened an Update Committee to conduct a comprehensive review of the peer-reviewed literature published since 2006 and to revise the guideline recommendations. The Update Committee developed new algorithms for testing and recommended quality assurance monitoring that would make *HER2* testing less variable and ensure more analytic consistency among laboratories.

Because there are important distinct differences in *HER2* expression, scoring, and outcomes in gastroesophageal adenocarcinoma (GEA) relative to breast carcinoma, the need for *HER2* guidelines (that include critical clinical and laboratory considerations) was recognized. CAP, the American Society for Clinical Pathology (ASCP), and ASCO convened an international Expert Panel to systematically review published documents and to develop an evidence-based guideline to establish recommendations for *HER2* testing in GEA.

Panel Composition

The CAP Pathology and Laboratory Quality Center, ASCP, and ASCO convened an international Expert Panel consisting of practicing pathologists, oncologists, and a gastroenterologist with expertise and experience in GEA. Members included practicing clinicians and pathologists from the United States, Canada, and Europe. CAP, ASCP, and ASCO approved the appointment of the project, co-chairs, and Expert Panel members. In addition, a physician-methodologist experienced in systematic review and guideline development consulted with the Panel throughout the project, and a patient advocate also participated to convey the patient experience.

The Expert Panel met face-to-face on April 25, 2015, to develop the scope and the key questions, and on August 29, 2015, to draft recommendations and assess the quality of evidence. The Panel met a total of 16 times via Web conference in small groups to review solicited feedback and finalize the recommendations. A nominal group technique was used by the panel for consensus decision making to encourage unique input with balanced participation among the group members. An open comment period was held from December 8, 2015, to January 11, 2016, during which draft recommendations were posted on the ASCP Web site. Twenty recommendations were drafted, with strong agreement for each recommendation from the open-comment-period participants ranging from 82% to 95%. The Web site received a total of 294 comments.

Teams of two Expert Panel members were assigned to two key questions and three to four draft recommendations to review all the comments received and provide an overall summary to the rest of the Panel. After Panel discussions, and the final quality of evidence assessment, the Panel members determined whether to maintain the original draft recommendations as is, or revise them with major content changes. Resolution of all changes was obtained by majority consensus of the Panel, using nominal group technique among the members. The Expert Panel approved the final recommendations by a formal vote.

Assessing the Strength of Recommendations

The guideline recommendations were crafted, in part, by using the GLIDES (Guidelines Into Decision Support) methodology and accompanying BridgeWiz software (Yale University, New Haven, CT). Development of recommendations required that the Expert Panel review and identify evidence and make a series of key judgments (using procedures described in the Data Supplement [see the "Availability of Companion Documents" field]). Additionally, the Expert Panel gave its recommendations with regard to potential clinical impact by assessing benefits and harms for each recommendation, and then rated the quality of evidence for the recommendations as high, intermediate, low, or insufficient. The

Grading of Recommendations Assessment, Development and Evaluation (GRADE) method was used to rate the quality of the evidence. CAP uses a three-tier system to rate the strength of recommendations instead of the traditional two-tier approach of strong or weak recommendations. This approach is consistent with prior CAP guidelines (see the "Rating Scheme for the Strength of the Recommendations" field).

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

CAP Designation	GLIDES Designation	Recommendation	Rationale
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Abbreviations: CAP, College of American Pathologists; GLIDES, Guidelines Into Decision Support; N/A, not applicable.

Cost Analysis

Formal cost analysis or cost effectiveness was not performed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Each organization instituted a review process to approve the guideline. The College of American Pathologists (CAP) convened an Independent Review Panel representing the Council for Scientific Affairs to review and approve the guideline. The Independent Review Panel was masked to the Expert Panel and vetted through the conflict of interest (COI) process. The American Society for Clinical Pathology (ASCP) assigned the review of the guideline to a Special Review Panel at the discretion of the ASCP Executive Office and Board of Directors. The American Society of Clinical Oncology (ASCO) approval process required the review and approval of the Clinical Practice Guidelines Committee.

The Clinical Practice Guidelines Committee approved this guideline on June 20, 2016.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

All patients who have documented advanced gastroesophageal adenocarcinoma (GEA) and who are considered good candidates for combination chemotherapy plus trastuzumab therapy should have their tumor tissue tested for *human epidermal growth factor receptor 2* (*HER2*) overexpression and/or amplification. In patients with *HER2*-positive GEA, the addition of trastuzumab can increase the response rate, prolong progression-free survival, and prolong overall survival. Other than providing guidance regarding the addition of trastuzumab to cytotoxic combination (when the tumor is *HER2* positive), *HER2* status provides little additional value such as prognostic or predictive information. Currently, there is no evidence of benefit of *HER2*-directed therapy in patients without advanced GEA.

Refer to the "Guideline Statements" section of the original guideline document for a discussion of the potential benefits of each recommendation.

Potential Harms

- False-positive or false-negative results of tests
- There is no documented benefit for starting *human epidermal growth factor receptor 2* (*HER2*)-directed treatment in the absence of confirmed *HER2* positivity, and there is an added potential for the patient to incur unnecessary adverse effects or costs.
- In the ToGA trial, patients were randomly assigned to receive capecitabine plus cisplatin or fluorouracil plus cisplatin in combination with trastuzumab. The cardiac adverse event rate was low (6%) and did not differ between the treatment groups. Trastuzumab was generally well tolerated, but the patients assigned to trastuzumab experienced slightly higher rates of diarrhea, stomatitis, anemia, thrombocytopenia, fatigue, and weight loss. However, there was no difference between the groups in adverse effect frequency, or grade 3 or 4 toxicities except for diarrhea.

Refer to the "Guideline Statements" section of the original guideline document for a discussion of any potential harms associated with each recommendation.

Qualifying Statements

Qualifying Statements

The College of American Pathologists (CAP) developed the Pathology and Laboratory Quality Center as a forum to create and maintain evidence-based practice guidelines and consensus statements. Practice guidelines and consensus statements reflect the best available evidence and expert consensus supported in practice. They are intended to assist physicians and patients in clinical decision making and to identify questions and settings for further research. With the rapid flow of scientific information, new evidence may emerge between the time a practice guideline or consensus statement is developed and when it is published or read. Guidelines and statements are not continually updated and may not reflect the most recent evidence. Guidelines and statements address only the topics specifically identified therein and are not applicable to other interventions, diseases, or stages of diseases. Furthermore, guidelines and consensus statements cannot account for individual variation among patients and cannot be considered inclusive of all proper methods of care or exclusive of other treatments. It is the responsibility of the treating physician or other health care provider, relying on independent experience and knowledge, to determine the best course of treatment for the patient. Accordingly, adherence to any practice guideline or consensus statement is voluntary, with the ultimate determination regarding its application to be made by the physician in light of each patient's individual circumstances and preferences. CAP, the American Society for Clinical Pathology (ASCP), and the American Society of Clinical Oncology (ASCO) make no warranty, express or implied, regarding guidelines and statements and specifically exclude any warranties of merchantability and fitness for a particular use or purpose. CAP, ASCP, and ASCO assume no responsibility for any injury or damage to persons or property arising out of or related to any use of this statement or for any errors or omissions.

Implementation of the Guideline

Description of Implementation Strategy

American Society of Clinical Oncology (ASCO) guidelines are developed for implementation across health settings. Barriers to implementation include the need to increase awareness of the guideline recommendations among front-line practitioners and survivors of cancer and caregivers, and also to provide adequate services in the face of limited resources. The Bottom Line Box included within the guideline was designed to facilitate implementation of recommendations. This guideline will be distributed widely through the ASCO Practice Guideline Implementation Network. ASCO guidelines are posted on the ASCO Web site and most often published in *Journal of Clinical Oncology* and *Journal of Oncology Practice*.

For information on the ASCO implementation strategy, please see the ASCO Web site .

Implementation Tools

Clinical Algorithm

Patient Resources

Pocket Guide/Reference Cards

Resources

Slide Presentation

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Bartley AN, Washington MK, Colasacco C, Ventura CB, Ismaila N, Benson AB III, Carrato A, Gulley ML, Jain D, Kakar S, Mackay HJ, Streutker C, Tang L, Troxell M, Ajani JA. HER2 testing and clinical decision making in gastroesophageal adenocarcinoma: guideline from the College of American Pathologists, American Society for Clinical Pathology, and the American Society of Clinical Oncology. J Clin Oncol. 2017 Feb 1;35(4):446-64. [131 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2017 Feb 1

Guideline Developer(s)

American Society for Clinical Pathology - Professional Association

American Society of Clinical Oncology - Medical Specialty Society

College of American Pathologists - Medical Specialty Society

Source(s) of Funding

The College of American Pathologists (CAP), the American Society for Clinical Pathology (ASCP), and the American Society of Clinical Oncology (ASCO) provided funding for the administration of the project; no industry funding was involved in any aspect of the development of this guideline. All panel members volunteered their time and were not compensated for their involvement.

Guideline Committee

Expert Panel

Composition of Group That Authored the Guideline

Expert Panel Members: Angela N. Bartley (*Co-chair*), St Joseph Mercy Hospital, Ann Arbor, MI; Mary Kay Washington (*Co-chair*), Vanderbilt University Medical Center, Nashville, TN; Carol Colasacco, College of American Pathologists, Northfield, IL; Christina B. Ventura, College of American Pathologists, Northfield, IL; Al B. Benson III, Northwestern University, Chicago, IL; Nofisat Ismaila, American Society of Clinical Oncology, Alexandria, VA; Alfredo Carrato, Ramón y Cajal University Hospital, Madrid, Spain; Margaret L. Gulley, University of North Carolina, Chapel Hill, NC; Dhanpat Jain, Yale University School of Medicine, New Haven, CT; Sanjay Kakar, University of California, San Francisco, CA; Helen J. Mackay, Princess Margaret Cancer Centre, Toronto, Canada; Catherine Streutker, St Michael's Hospital, University of Toronto, Toronto, Canada; Laura Tang, Memorial Sloan Kettering Cancer Center, New York, NY; Megan Troxell, Stanford University Medical Center, Stanford, CA; Jaffer A. Ajani (*Co-chair*), The University of Texas MD Anderson Cancer Center, Houston, TX

Financial Disclosures/Conflicts of Interest

Conflict of Interest Policy

Before appointment to the Expert Panel, potential members completed a joint conflict of interest (COI) disclosure process whose policy and form require disclosure of material financial interest in, or potential for benefit of significant value from, the guideline's development or its recommendations. The potential members completed the COI disclosure form, listing any relationship that could be interpreted as constituting an actual, potential, or apparent conflict. Potential conflicts were managed by the co-chairs. All members were required to disclose conflicts before beginning the project and then continuously throughout the project's timeline. Disclosed conflicts of the Expert Panel members are listed below. All panel members volunteered their time and were not compensated for their involvement. Please see the Data Supplement (for details on the COI policy (see the "Availability of Companion Documents" field).

Authors' Disclosures of Potential Conflicts of Interest

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of

this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/site/ifc.

Angela N. Bartley
No relationship to disclose

Mary Kay Washington
No relationship to disclose

Carol Colasacco
No relationship to disclose

Christina B. Ventura
No relationship to disclose

Nofisat Ismaila
No relationship to disclose

Al B. Benson III
Consulting or Advisory Role: Genentech/Roche, Sanofi, Bristol-Myers Squibb, Merck Serono, Merck/Schering Plough, Spectrum Pharmaceuticals, Lilly/ImClone, Celgene, Genomic Health, National Cancer Institute, Vicus Therapeutics, Pharmacyclics, Precision Therapeutics, Taiho Pharmaceutical, Bayer, Alchemia, Infinity Pharmaceuticals, Boehringer Ingelheim, Astellas Pharma, EMD Serono, IntegraGen
Research Funding: Genentech (I), Gilead Sciences, Amgen, Astellas Pharma, Advanced Accelerator Applications, Bayer/Onyx, Novartis, Alchemia, AVEO, Infinity Pharmaceuticals, Merck Serono (Inst), EMD Serono (Inst)
Travel, Accommodations, Expenses: Genentech/Roche, Lilly/ImClone, Bayer, Sanofi, Spectrum Pharmaceuticals, AVEO, Gilead Sciences, Astellas Pharma

Alfredo Carrato
Consulting or Advisory Role: Roche, Bayer, Merck, Sanofi, Celgene, Amgen, Bristol-Myers Squibb, Merck Sharp & Dohme Oncology, Baxalta
Speakers' Bureau: Bayer, Merck, Celgene, Amgen
Travel, Accommodations, Expenses: Roche, Merck, Celgene

Margaret L. Gulley
Consulting or Advisory Role: Beacon LBS, McKesson
Research Funding: Illumina

Dhanpat Jain
No relationship to disclose

Sanjay Kakar
No relationship to disclose

Helen J. Mackay
No relationship to disclose

Catherine Streutker
No relationship to disclose

Laura Tang
No relationship to disclose

Megan Troxell
Honoraria: Ventana Medical Systems

Jaffer A. Ajani
Honoraria: Lilly/ImClone, Bayer, Novartis, Five Prime Therapeutics, Taiho Pharmaceutical, Genentech, Celgene
Research Funding: Novartis, Bristol-Myers Squibb, Taiho Pharmaceutical, Roche/Genentech, MedImmune, Amgen, Lilly/Imclone, Merck, Delta-Fly Pharma, Gilead Sciences, Takeda, Celgene
Patents, Royalties, Other Intellectual Property: I have research funding from: Genentech, Roche, BMS, Taiho, MedImmune, Merck, Amgen, Lilly
Travel, Accommodations, Expenses: Novartis, Bayer, Five Prime Therapeutics

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the Journal of Clinical Oncology Web site.

Availability of Companion Documents

The following are available:

- HER2 testing and clinical decision making in gastroesophageal adenocarcinoma: guideline from the College of American Pathologists, American Society for Clinical Pathology, and American Society of Clinical Oncology. Data supplement. Alexandria (VA): American Society of Clinical Oncology; 2017. 32 p. Available from the American Society of Clinical Oncology (ASCO) Web site.
- HER2 testing and clinical decision making in gastroesophageal adenocarcinoma: guideline from the College of American Pathologists, American Society for Clinical Pathology, and American Society of Clinical Oncology. Slide set. Alexandria (VA): American Society of Clinical Oncology; 2017. 16 p. Available from the ASCO Web site.
- HER2 testing and clinical decision making in gastroesophageal adenocarcinoma: guideline from the College of American Pathologists, American Society for Clinical Pathology, and American Society of Clinical Oncology. Summary of recommendations. Alexandria (VA): American Society of Clinical Oncology; 2017. 1 p. Available from the ASCO Web site.
- HER2 testing and clinical decision making in gastroesophageal adenocarcinoma: guideline from the College of American Pathologists, American Society for Clinical Pathology, and American Society of Clinical Oncology. Frequently asked questions. Alexandria (VA): American Society of Clinical Oncology; 10 Nov 2016. 2 p. Available from the ASCO Web site.
- HER2 testing and clinical decision making in gastroesophageal adenocarcinoma: guideline from the College of American Pathologists, American Society for Clinical Pathology, and American Society of Clinical Oncology. Video. Available from the ASCO Web site.

Patient Resources

The following are available:

- Esophageal cancer. Patient information. 2017. Available from the Cancer.Net Web site.
- Stomach cancer. Patient information. 2017. Available from the Cancer.Net Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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